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(21) International Application Number: PCT/EP98/01423 (22) International Filing Date: 10 March 1998 (10.03.98) (30) Priority Data: 60/039,378 20 March 1997 (20.03.97) US 60/072,355 23 January 1998 (23.01.98) US (71) Applicant (for AU BB CA GB GH GM IE IL KE LC LK LS MN MW NZ SD SG SL SZ TT UG ZW only): UNILEVER PLC [GB/GB]; Unilever House, Blackfriars, London EC4P 4BQ (GB). (71) Applicant (for all designated States except AU BB CA GB GH GM IE IL KE LC LK LS MN MW NZ SD SG SL SZ TT UG ZW): UNILEVER N.V. [NL/NL]; Weena 455, NL-3013 AL Rotterdam (NL).		(72) Inventors: CROTTY, Brian, Andrew; 46 Damascus Road, Branford, CT 06405 (US). MINER, Philip, Edward; 25 Cannon Drive, Newtown, CT 06470 (US). JOHNSON, Anthony, William; 211 Papermill Lane, Fairfield, CT 06430 (US). ZNAIDEN, Alexander, Paul; 110 Fox Road, Trumbull, CT 06611 (US). COREY, Joseph, Michael; 108 Holly Street, Waterbury, CT 06706 (US). VARGAS, Anthony; 58 Georges Lane, Monroe, CT 06468 (US). MEYERS, Alan, Joel; 68 Frederick Street, Trumbull, CT 06611 (US). LANGE, Beth, Anne; 319 Main Avenue, Woodridge, NJ 07075 (US). (74) Agent: ROTS, Maria, Johanna, Francisca; Unilever plc, Patent Division, Colworth House, Sharnbrook, Bedford MK44 1LQ (GB). (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: COSMETIC PRODUCT (57) Abstract <p>A cosmetic product is provided for delivery of skin actives through adhesive strips which concurrently remove keratotic plugs from skin pores. The product is a strip including a flexible substrate sheet onto which a composition containing an adhesive polymer is deposited. The composition is essentially a polymer of anionic, cationic, nonionic, amphoteric or zwitterionic variety which increases in tackiness upon being wetted, with wetting occurring just prior to application onto the skin thereby enhancing the composition's adhesivity. Skin agents delivered through the adhesive strip include vitamins, herbal extracts, alpha- and beta-hydroxycarboxylic acids, ceramides, anti-inflammatories, antimicrobials, vasoconstrictors, zinc salts and mixtures thereof. The strips are sealably enclosed within a pouch for purposes of moisture protection.</p>		

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COSMETIC PRODUCT

BACKGROUND OF THE INVENTION

5 Field of the Invention

The invention concerns a cosmetic product applied to the skin for removing keratotic plugs from pores and concurrent delivery of skin benefit agents.

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The Related Art

A variety of vehicles exist for delivery of actives to the skin. These vehicles may be lotions, creams, pads, sprays
15 and even masks. Some are leave-on systems while others are intended as short-lived wash-off products. Those who practice cosmetic arts know the critical role that vehicles perform in delivering actives effectively to skin.

20 Delivery is not the only concern. Some types of actives are degraded by the vehicle. For instance, ascorbic acid, also known by its common name of Vitamin C, is a very unstable substance. Although readily soluble in water, rapid
25 oxidation occurs in aqueous media. Solubility of ascorbic acid has been reported to be relatively poor in nonaqueous media, thereby preventing an anhydrous system from achieving a significant level of active concentration. Derivatives have been produced with greater stability than the parent component. See U.S. Patent 5,137,723 (Yamamoto et al.) and
30 U.S. Patent 5,078,989 (Ando et al.). A two-pack approach has been developed where Vitamin C powder and other ingredients are separately packaged in different containers with mixing just prior to use. See U.S. Patent 4,818,521 (Tamabuchi).

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plugs as well as a layer of skin. These products do not contain any skin benefit agents. In fact, the whole concept behind the strips is removal rather than deposition.

- 5 It is an object of the present invention to provide a delivery system for vitamins, herbal extracts and hydroxycarboxylic acids which assists penetration of these actives into the human skin.
- 10 Another object of the present invention is to provide a delivery system for vitamins, herbal extracts and hydroxycarboxylic acids which does not interfere or degrade the active during storage.
- 15 These and other objects of the present invention will become more readily apparent through the following summary, detailed discussion and examples.

SUMMARY OF THE INVENTION

20

A cosmetic product for delivery of skin actives is provided which includes:

(A) a strip including:

25

- (i) a flexible substrate sheet; and
 - (ii) a composition containing a polymer selected from the group consisting of anionic, cationic, nonionic, amphoteric, zwitterionic and polymer mixtures thereof deposited onto the substrate
- 30 sheet, the composition further including an active selected from the group consisting of vitamins, herbal extracts, alpha- and beta-hydroxycarboxylic acids, ceramides, anti-
- 35 inflammatories, antimicrobials, vasoconstrictors,

- 5 -

Vitamin A for purposes of this invention include retinol, retinoic acid as well as retinyl C₁-C₂₂ fatty acid esters. Most preferred among the esters are retinyl palmitate and retinyl linoleate. Vitamin E may be provided in the form of

5 tocotrienols, α -tocopherol, β -tocopherol, γ -tocopherol and δ -tocopherol. Included within the Vitamin E group are tocopheryl C₁-C₂₂ fatty acid esters including tocopheryl acetate, tocopherol linoleate and tocopheryl palmitate. Vitamin B may be present in the form of thiamine,

10 riboflavin, niacin, pantothenic acid, biotin, cobalamin, pyridoxine hydrochloric, pyridoxamine dihydrochloride, pyridoxal, pyridoxal phosphate, folic acid, inositol and mixtures as well as complexes thereof. Under the term vitamin may also be included thaprolone, L-caritine,

15 nicotinic acid, nicotinamide and cyproterone acetate.

Herbal extracts particularly suitable for the present invention are antioxidants or free-radical inhibitors. Examples of these extracts include:

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quercetin	o
rutin	w
morin	w
kaempferol	o
myricetin	w/o
genistein	o
Phytoestrogen Extracts	
coumestrol	o
estriol	o
phytosterols	o
Other Extracts	
limonene	o
ethoxyquin	o
chlorogenic acid	w
glutathione	w
hydroquinone	o
ubiquinone (coenzyme Q)	o
lipoic acid	o
N-acetyl cysteine	o
curcumin	o

Herbal extracts particularly effective for sebum/oil control include dill, horseradish, oats, neem, beet, broccoli, tea, pumpkin, soybean, barley, walnut, flax, ginseng, poppy, avocado, pea, sesame, dandelion, wheat, nettle, cashew, pineapple, apple, asparagus, Brazilnut, chickpea, grapefruit, orange, cucumber, buckwheat, strawberry, ginko, tomato, blueberry, cowpea and grape extracts.

Other herbal extracts also suitable are those of ivy horse chestnut, centella asiatica, rosmarinic acid, glycyrrizinate derivatives, alpha bisabolol, azulene and derivatives thereof, asiaticoside, sericoside, ruscogenin, escin, escolin, betulinic acid and derivatives thereof, catechin and derivatives thereof.

Alpha- and beta- hydroxycarboxylic acids ranging from C₁-C₁₀ are also suitably delivered by the adhesive strips of the present invention. The beta-hydroxycarboxylic acids are primarily exemplified by salicylic acid and C₁-C₁₀ ester and

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salts) are also meant to be included within the term "alpha- and beta- hydroxycarboxylic acid". Depending on the pH of the composition, a mixture of the salt and the acid may be present.

5

The preferred alpha hydroxycarboxylic acids are monocarboxylic acids, in order to improve skin penetration and efficacy.

10 Even more preferably, the hydroxy acid is chosen from lactic acid, glycolic acid, mandelic acid, and mixtures thereof to optimize the efficacy of compositions by increasing percutaneous absorption. Most preferred is the L-form of an alpha hydroxycarboxylic acid.

15

Ceramides useful for the present invention are sphingolipids or phytosphingolipids including Ceramide 1, Ceramide 3 and Ceramide 6.

20 Anti-inflammatories of the present invention are illustrated by corticoids such as beta-methasone 17-acetate, indomethacin, ketoprofen, flufenamic acid, ibuprofen, diclofenace, diflunisal, fenclofenac, naproxen, piroxidam and sulindac. Antimicrobials illustrative of the present
25 invention include, chlorohexidine, hexetidine, 3,4,4'-trichlorocarbanilide, (tricarbanilide) 2,4,4'-trichloro-2-hydroxydiphenyl ether (triclosan), cetyl pyridinium chloride, benzalkonium chloride, C₂-C₂₀ organoperoxy compounds (e.g. benzoyl peroxide) and mixtures. Vasoconstrictors are
30 illustrated by compounds such as papaverine, yohimbine, visnadin, khellin, bebellin and nicotinate derivatives. Zinc salts which may be effective include zinc thaproline, zinc chloride, zinc sulfate, zinc phenolsulfonate and zinc pyrithione. Other substances within one or more of the

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or polypropylene sheets, several layers of which can be laminated together. These layers may also be provided with a coating of wax or other volatile fluid impermeable material.

5

The product is used by removing the strip from its usually individually wrapped pouch and either directly wetting the composition on the sheet or indirectly by wetting the face in areas to be contacted by the composition. In either
10 instance, the wetting agent interacts with the composition so it becomes tacky and sufficiently mobile to flow into skin pores. The time between removal of strip from the pouch and use may be anywhere from 5 seconds to several hours, usually from 10 to 20 seconds. Pure water is the
15 preferred wetting agent. However, other liquid systems or gels could be employed. Suitable wetting agents would include alcohols such as ethanol, propanol, propylene glycol, polyethylene glycol, polypropylene glycol and especially mixtures of these alcohols with water. Gels
20 would normally consist of structured liquids (particularly water) thickened with structuring agents such as Carbomer.

Subsequent to wetting, the composition is allowed to dry over the area of treatment. During drying the keratotic
25 plugs stickingly adhere to the composition. Advantageously the drying period ranges from 1 minute to 5 hours, preferably from 5 minutes to 1 hour, optimally from 10 to 20 minutes. Thereafter, the dried composition with adhered plugs is peeled from the skin.

30

Mobility of the composition may be measured by yield point. The yield point should range from 1 to 400 Pascals, preferably from 20 to 200, optimally from 50 to 100 Pascals

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N-vinylpyrrolidone with compatible nonionic monomers such as vinyl acetate and terpolymers of ethyl acrylate, butyl methacrylate and methyl methacrylate. Nonionic polymers containing N-vinylpyrrolidone in various weight average
5 molecular weights are available commercially from ISP Corporation such as homopolymers of N-vinylpyrrolidone having an average molecular weight of about 630,000 under the trademark PVP K-90 and those having an average molecular weight of about 1,000,000 sold under the trademark of PVP
10 K-120. Particularly preferred is poly(methyl vinyl ether/maleic anhydride) as an unneutralized resin available from ISP Corporation under the trademark Gantrez® S-97 BF.

Anionic adhesive polymers often are derived from the
15 nonionic types which include carboxylic acid functions. Alkaline agents are employed to neutralize the carboxylic acid or anhydride transforming them into anionic salts. Examples of suitable neutralizing agents include
2-amino-2-methyl-1,3-propanediol (AMPD);
20 2-amino-2-ethyl-1,3-propanediol (AEPD);
2-amino-2-methyl-1-propanol (AMP); 2-amino-1-butanol (AB);
monoethanolamine (MEA); diethanolamine (DEA);
triethanolamine (TEA); monoisopropanolamine (MIPA);
diisopropanol-amine (DIPA); triisopropanolamine (TIPA); and
25 dimethyl stearamine (DMS). Most preferred is AMP.

Particularly preferred anionic polymers are the salts of poly(methyl vinyl ether/maleic anhydride) and polystyrene sulfonic acid. The former is obtained by at least partial
30 neutralization of Gantrez® S-97 BF and the latter available from the National Starch & Chemical Company under the trademarks Versa TL-501 and Flexan® 130 having respective molecular weights of about 500,000 and 100,000. Other polymer films which may be employed and are commercially
35 available as listed in the Table below.

- 15 -

Dimethylaminostyrene (DMASt) and Dimethyaminomethylstyrene (DMAMSt) and the like which are styrenes having a dialkylamino group;

- 5 4-Vinyl pyridine and 2-vinyl pyridine which are vinyl pyridines; and

Quaternized products of these with a known quaternizing agent such as alkyl halide, benzyl halide, alkyl or aryl
10 sulfonic acid, or dialkyl sulfate.

Among suitable amphoteric adhesive polymers are those derived from monomers such as:

- 15 N-(3-sulfopropyl)-N-acryloyloxyethyl-N,N-dimethylammonium betaine, N-(3-sulfopropyl)-N-methacroylamidepropyl-N,N-dimethylammonium betaine, N-(3-carboxymethyl)-N-methacroylamidepropyl-N,N-dimethylammonium betaine and N-carboxymethyl-N-methacroyloxyethyl-N,N-dimethylammonium
20 betaine.

When the salt forming group of the cationic and amphoteric polymers is not ionized, it is preferred to ionize it via neutralization with known acids such as hydrochloric acid
25 and sulfuric acid which are inorganic acids; acetic acid, propionic acid, lactic acid, succinic acid, glycol acid which are organic acids, or with known bases such as triethylamine, trimethylamine which are tertiary amines; ammonia; or sodium hydroxide.

30

Most polymers suitable for the present invention will be relatively brittle when dried. Therefore, they require a supporting surface which is a flexible substrate sheet. Substrate sheets of the present invention may either be
35 occlusive or non-occlusive. Preferably but not necessarily

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EXAMPLE 1

A variety of polymers were evaluated for their adhesive effects in removing keratotic plugs from the skin. The polymers listed in Table I below were coated onto a non-woven resin bonded rayon (1 ounce/square yard). A knife-over-roll was utilized in the coating operation. After coating, the non-woven polymer impregnated substrate sheets were dried at 75°C in a convection oven. They were then cut into small patches.

The test patches were applied to the face of panelists in an area containing several plugged pores. The plugged pores were counted. Water was applied to the patch and it was then placed over the test area with wet side down. Next, the patch was allowed to dry whereupon it was peeled off. The number of plugs removed were counted as they appeared on the adhesive patch. Percentage of plugs removed were calculated to reflect efficiency of the test product.

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TABLE II

NONWOVEN	% PLUGS PULLED	OBSERVATIONS
PGI 5255 Rayon Resin bonded (1 oz./sq. yard)	90-100	Nice appearance
Veratec 9408810 Polyester/cellulose Wet laid (1.2 oz/sq. yard)	70-100	Nice appearance: Nonwoven may be too weak
Veratec 2006094 Polypropylene Thermal Bond (.6 oz/sq. yard)	40-60	Nice appearance
Veratec Polyethylene (.5 oz/sq. yard)	10	Poor appearance: When used in application adhesive dried very slow.

5 EXAMPLE 3

The following experiments were conducted to demonstrate the efficacy of employing adhesive strips activated just prior to use by water in the delivery of skin benefiting agents.

- 10 More particularly, the experiments reported herein concerned delivery of Vitamin C for anti-oxidant benefits.

Lipid Peroxidation Test For Anti-Oxidant Activity

- 15 A vulnerable target for free radicals in facial skin is the lipids. Lipid peroxidation can lead to membrane fluidity changes, altered activity of membrane-bound enzymes and receptors, changes in ion permeability, protein and DNA damage and mutagenesis, which may contribute to attributes
- 20 of unhealthy skin. Lipid peroxidation can be induced in skin by UV radiation, ozone, environmental pollutants and

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isopropanol in a test tube. The test tube was vortexed until the Sebutape was saturated. It was then analyzed for lipid hydroperoxide content using the K-Assay LPO-CC assay kit (Kamiya Biochemical Company, Seattle WA). The assay

5 measures lipid hydroxyperoxides as follows: In the presence of hemoglobin, lipid hydroperoxides are reduced to hydroxyl derivatives (lipid alcohols) and the 10-N-Methylcarbamoyl-3, 7-dimethylamino-10 H-phenothiazine (MCDP) chromagen is

10 oxidatively cleaved to form methylene blue in an equal molar reaction. Lipid peroxides are then quantitated colorimetrically measuring the methylene blue at 675 nm (Kamiya Biochemical Company, assay protocol). LPO values are calculated according to the following equation:

$$15 \quad \text{LPO (nmol/ml)} = \frac{(\text{Absorbance SAMPLE} - \text{Absorbance BLANK})}{(\text{Absorbance STANDARD} - \text{Absorbance BLANK})} \times 50$$

Results of the test are recorded under Table III.

20 **TABLE III**

PANELIST	30 MINUTES POST		1 HOUR POST		3 HOUR POST	
	BLANK	3% ASCORBATE	BLANK	3% ASCORBATE	BLANK	3% ASCORBATE
1	72	98.4	47.9	68.9	90.4	69.3
2	39.2	70.4	54.3	43.1	139.5	202.6
	BLANK	6% ASCORBATE	BLANK	6% ASCORBATE	BLANK	6% ASCORBATE
3	24	32	18.1	25	29.8	23.7
4	39.2	52.8	75.9	44.8	315.8	109.6

In the 30 minute sample, all of the four panelists had lower

25 lipid hydroxyperoxide values on the control strip than on the ascorbate treated side. This result is believed to occur because the control adhered better than the ascorbate containing strips, thus pulling more lipids from the skin. In the one hour sample, two of the four panelists on their

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CLAIMS

1. A cosmetic product for delivery of skin actives is provided which includes:

5

(A) a strip comprising:

(i) a flexible substrate sheet; and

(ii) a composition containing a polymer

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selected from the group consisting of anionic, cationic, nonionic, amphoteric, zwitterionic and polymer mixtures thereof deposited onto the substrate sheet, the composition further comprising an active selected from the group consisting of vitamins, herbal extracts, alpha- and beta- hydroxycarboxylic acids, ceramides, anti-inflammatories, antimicrobials, vasoconstrictors, zinc salts and mixtures thereof; the composition increasing in tackiness upon being wetted just prior to use thereby enhancing the composition adhesivity to skin; and

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(B) a pouch sealably enclosing the strip.

2. The product according to claim 1 wherein the vitamins selected from the group consisting of Vitamin A, Vitamin B, Vitamin C, Vitamin E and combinations thereof.

30

3. The product according to claim 2 wherein the Vitamin C is selected from the group consisting of ascorbic acid, magnesium ascorbyl phosphate, ascorbyl palmitate, L-

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 98/01423

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61K7/48 A61K7/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4 762 124 A (KERCH MARTHA E ET AL) 9 August 1988 see the whole document	1-3,5
P, Y	WO 97 32567 A (KAO CORP ; ISHIDA KOICHI (JP); KANEDA MANABU (JP); KOMORI YASUHIRO) 12 September 1997 see table 1 see claims 1-6, 12-15 see page 40, line 5-16 see page 24, line 2-15 see page 20, line 1-18 see page 19, line 20-25 see page 18, line 6-15 see page 1-13	1-3,5

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
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- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

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- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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